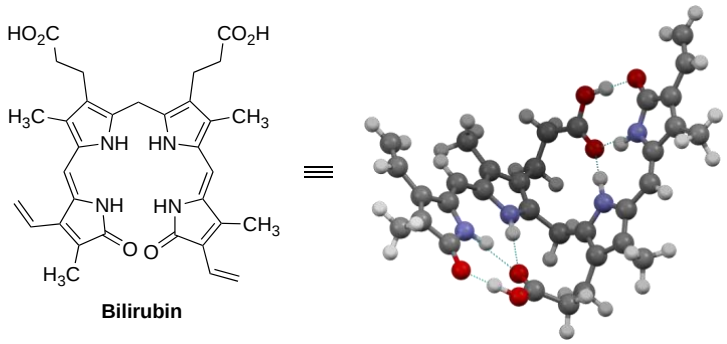
Development of a Unified Synthetic Approach to the Oxidation Products of Bilirubin

Taufiqueahmed Mujawar [a]; Petr Sevelda [a]; Jakub Švenda* [a, b]

[a] *Masaryk University, Faculty of Science, Department of Chemistry, Kamenice 5/A8, 623 00*

Brno, Czech Republic
[b] *International Clinical Research Center, St. Anne's University Hospital Brno, Pekařská 53, 656 91 Brno, Czech Republic*
mtaufiqueahmed@sci.muni.cz; svenda@chemi.muni.cz



Bilirubin

Yellow pigment bilirubin is the well-known primary product of heme catabolism.[1] It is a powerful antioxidant[2] and a potent signaling molecule[3] with multiple speculated biological functions. When exceeding safe levels in the blood, particularly during the neonatal period, severe hyperbilirubinemia can result and lead to neurotoxicity accounting for some instances of neonatal morbidity and mortality.[4] Despite the worldwide use of phototherapy and numerous scientific studies thereof, there remain important unanswered questions. Bilirubin is a potent antioxidant and gives rise to various products of (photo)oxidation.[5–7] Standards of such bilirubin-derived products are needed for studies of their inherent bioactivities and mechanisms of formation. Unfortunately, accessing these in sufficient quantities and purity is often problematic. The main objective of our work is to develop a unified synthetic platform that will deliver all major classes of bilirubin-derived oxidation products. Recently, the approach featuring pre-functionalized building blocks and metal-catalyzed transformations has allowed us to prepare simple and complex products of oxidative degradation of bilirubin.

Keywords: bilirubin, (photo)oxidation products, chemical synthesis

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